is that protein in the body constitutes only 15 percent of total energy stores, and depletion of a half to a third of these stores is incompatible with life. Because we have neither an exact means of predicting this point during a fast, nor of determining individual vulnerability to protein loss during prolonged periods of fasting, starvation (in excess of several days) to reduce weight should probably be avoided.

A second point of importance that militates against using prolonged fasting for weight loss is the simple fact that it becomes a less effective means of weight loss the longer the fast is maintained. This is nicely shown in the single patient studied by Kerndt and associates. The rate of weight loss in the patient was 0.9 kg per day during the first five days of fasting. By the third week it was 0.3 kg per day, and one can safely predict that it would be even less by the fourth or fifth week. Two important adjustments occur during fasting that change the rate at which body weight is reduced: First, serum triiodothyronine (T_3) concentrations decrease during fasting such that they reach levels recorded in the hypothyroid state.[2,3] Associated with the decrease of T_3 is a concomitant lowering of the basal metabolic rate. The latter phenomenon was actually recognized by investigators many years before the development of means of measuring T_3. The change in the T_3 level is an important adaptive mechanism that assures that the body burns only that fuel which is necessary for the most essential functions. In essence, the thermostat is turned down.

Second, ketosis itself, a phenomenon considered in detail in this study, induces changes in ketone excretion. Ketosis results in a reduced capacity of the kidney to excrete ketones, which in turn permits a decrease in the mobilization of free fatty acids.[4] In essence, ketones remain available over a longer period of time for fuel usage. These two changes limit body weight loss during the later phases of a fast from a third to a fourth of that achieved during the initial phase of fasting.

The findings on multiple diagnostic tests can be altered by fasting, and this general fact requires emphasis. Changes in the serum concentrations of hormones not directly related to balancing substrates are well documented. The levels of follicle-stimulating hormone and luteinizing hormone, for example, clearly decrease during fasting, along with changes in T_3, insulin and glucagon levels. A failure to appreciate this leads to ridiculous conclusions by the uninformed.

One is reminded of the situation in which an intern and a resident ordered thyroid function studies on the same patient. The resident ordered a T_4 and the intern ordered a T_3. When the results of the T_4 returned, they were compatible with mild hyperthyroidism. When the T_3 findings returned, the intern began treating the patient for hypothyroidism. In general, any condition in which starvation plays a prominent role can be expected to yield a plethora of abnormal laboratory values which, if considered in a simplistic fashion, lead to erroneous and often ludicrous conclusions.

The basic information summarized in this review can provide practitioners with multiple insights into clinical problems. Because the review is of necessity somewhat encyclopedic, it might, like fasting, be reconsidered in small sections.

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REFERENCES

1. Cahill GF Jr, Herrera MG, Morgan AP, et al: Hormone-fuel interrelationships during fasting. J Clin Invest 1966 Nov; 45: 1751-1769

2. Portnay GI, O'Brian JT, Bush J, et al: The effect of starvation on the concentration and binding of thyroxine and triiodothyronine in serum and on response to TRH. J Clin Endocrinol Metab 1974 Jul; 39:191-194

3. Spaulding SW, Chopra IJ, Sherwin RS, et al: Effect of caloric restriction and dietary composition of serum T_3 and reverse T_4 in man. J Clin Endocrinol Metab 1976 Jan; 42:197-200

4. Sapir DG, Owen OE: Renal conservation of ketone bodies during starvation. Metabolism 1975 Jan; 24:23-33

Acquired Immune Dysfunction in Homosexual Men

IT IS WELL ESTABLISHED that a severe acquired immunodeficiency syndrome is occurring with increasing frequency among homosexual men.[1-3] The dramatic presentation of these cases leaves little doubt that this is a new syndrome and not a previously unrecognized disorder. Elsewhere in this issue Dr. Jeffrey Golden presents the clinical features of six homosexual men with *Pneumocystis carinii* infection. One of these patients died and the others are under follow-up evaluation. Clinical studies and long-term evaluation will be essentiai to determine whether there can be significant clinical and immunologic recovery from the acquired immunodeficiency found in these patients.

The cause of the acquired immunodeficiency in

homosexual men is not clear. Multiple factors have been implicated including drug use (marijuana, amyl nitrite and other agents), specific infectious agents such as hepatitis virus and cytomegalovirus, immunosuppressive effects of multiple simultaneous infectious agents and factors related to the homosexual life-style including oral-anal sexual contact and promiscuity.[4] It is unlikely that any single factor will emerge as the sole agent responsible for this severe acquired immunodeficiency.

What is most striking about the acquired immunodeficiency in homosexual men is its severity. Those persons in whom opportunistic infections develop have T-cell immunity that is less than 10 percent of normal. This degree of immunodeficiency usually occurs only in primary congenital immunodeficiency disorders. This degree of immunosuppression does not develop even in patients who receive radiation therapy or immunosuppressive therapy for malignancy. Immunologic abnormalities in acquired immunodeficiency in homosexual men include severely depressed T-cell numbers, a pronounced suppression of helper T cells associated with a concomitant increase in suppressor T cells and an abnormal response of lymphocytes to mitogens, allogenic cells and antigens.[1-3] Although immunoglobulin levels are normal to elevated, there is preliminary evidence that the severe T-cell impairment may also result in abnormal B-cell immunity.

Cytomegalovirus infection has received major attention as a possible infectious agent responsible for acquired immunodeficiency. The virus is strongly implicated as a cause of Kaposi's sarcoma in the homosexual population and virtually all homosexual men have evidence of continuing excretion of this virus. Repeated infection with cytomegalovirus alone, or in conjunction with other viruses, could result in rapid loss of T-cell function with susceptibility to opportunistic infection or malignancy.

Loss of immunologic function or immunologic attrition ordinarily occurs with aging. Thymic involution begins during teenage years and laboratory evidence of reduced T-cell immunity appears somewhere beyond 65 years of age.[5] In normal aging, the profile of immunologic attrition is similar to that found in acquired immunodeficiency in homosexual men, although the severity is not as great. It appears that the homosexual population is susceptible to an accelerated immunologic attrition that begins early in life and may be complete by age 35 to 45. Accumulating evidence suggests that the acquired immunodeficiency in the homosexual population is a result of repeated infection with the same or multiple viral agents. Even apparently healthy homosexual control populations have evidence of immunologic dysregulation as evidenced by reversed helper T-cell and suppressor T-cell ratios.[6,7] Transient reversal of helper-suppressor T-cell ratios occurs in nonhomosexual populations following viral infections, in particular hepatitis and cytomegalovirus.[8,9] However, in nonhomosexual populations, return of immunologic function occurs two to four weeks following acute viral infection. In the homosexual population it is possible that repeated viral infection, superimposed on an immunosuppressive state from a previous viral infection, could result in accelerated immunologic attrition.

As yet, there is no evidence to suggest that the acquired immunodeficiency found in homosexual men is reversible. Long-term follow-up studies of patients will be required to ascertain if clinical and laboratory improvement occurs spontaneously.

A number of approaches toward the treatment of patients with acquired immunodeficiency can be used. Patients with a known history of *Pneumocystis carinii* pneumonia or patients with documented severe immunodeficiency should receive trimethoprim-sulfamethoxazole therapy directed toward the prevention of *Pneumocystis carinii*. Patients with severe immunosuppression are probably also susceptible to fatal graft versus host reaction following transfusion of unirradiated blood products.[10] Therefore, all blood products administered to these patients should be irradiated to prevent this complication.[11] In addition, as blood products are known to transmit a variety of infectious agents, blood products should be selected from donors who are negative for antibodies to certain viruses such as hepatitis and cytomegalovirus.[12] If acquired immunodeficiency is related to multiple and repeated infections, then alteration of life-style with reduced frequency and types of exposures would be appropriate. Therapy with antiviral agents offers little promise because of the limited spectrum of antiviral activity as well as the emergence of resistant strains of virus. Active immunization directed toward specific viral agents such as hepatitis would be an important approach toward the prevention of infection. A new experimental cytomegalovirus

vaccine may become available in the future. Passive therapy directed toward the prevention of multiple infections should be evaluated. Gammaglobulin, in particular intravenous gammaglobulin, administered regularly has been associated with significant reduction in infection in primary immunodeficiency disorders.[13]

Immunotherapy, directed toward the reconstitution of T-cell immunity, offers potential in severely immunosuppressed patients. Aggressive therapy consisting of thymus transplantation or bone marrow transplantation has significant risk in patients with multiple infections. A number of thymic factors have been evaluated in primary immunodeficiency disorders and are being considered for patients with acquired immunodeficiency disease.[14] It is possible, however, that the degree of immunologic impairment has gone beyond that which can be reconstituted by thymic factor therapy.

Future studies should be directed toward ascertaining the specific causes of the acquired immunodeficiency, the potential spontaneous reversibility of the immunodeficiency and therapy capable of providing additional protection against immunologic attrition as well as reconstitution of immunity.

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REFERENCES

1. Gottlieb MS, Schroff R, Schanker HM, et al: Pneumocystis carinii pneumonia and mucosal candidiasis in previously healthy homosexual men. N Engl J Med 1981; 305:1425-1444

2. Durack DT: Opportunistic infections and Kaposi's sarcoma in homosexual men. N Engl J Med 1981; 305:1465-1468

3. Masur H, Michelia MA, Greene JB, et al: Outbreak of Kaposi's sarcoma with cytomegalovirus infection in young homosexual men. Am J Med 1981; 305:1431-1438

4. Auerbach DM: Special Report: Epidemiologic aspects of the current outbreak of Kaposi's sarcoma and opportunistic infections. N Engl J Med 1982; 306:248-252

5. Makinodan T: Mechanism of senescence of the immune response. Fed Proc 1978 Apr; 37:1239-1240

6. Wallace JI, Coral FS, Rimm IJ, et al: T-cell ratios in homosexuals. Lancet 1982; 1:908

7. Stahl R, Friedman-Kein C, Dubin D, et al: Immunologic abnormalities in homosexual men. Am J Med 1982; 73:171-178

8. Bach MA, Bach JF: Imbalance of T-cell subsets in human diseases. Int J Immunopharm 1981; 3:269-273

9. Thomas HC: T-cell subsets in patients with acute and chronic HBV infection. Int J Immunopharm 1981; 3:301-305

10. Wara DW, Brunner WC, Ammann AJ: Graft vs host disease, *In* Current Problems in Pediatrics. Chicago, Year Book Medical Publishers Inc, 1978 May

11. Ammann AJ, Fudenberg HH: Immunodeficiency diseases, *In* Stites DP, Stobo JD, Fudenberg HH, et al (Eds): Basic and Clinical Immunology, 4th Ed. Los Altos, CA, Lange Publications, 1982, pp 395-429

12. Winston DJ, Ito WG, Howell CL: Cytomegalovirus infections associated with leukocyte transfusions. Ann Intern Med 1980; 93:671-675

13. Ammann AJ, Ashman RF, Buckley RH, et al: Use of intravenous gammaglobulin in antibody immunodeficiency: Results of a multicenter controlled trial. Clin Immuno Immunopathol 1982 22:60-67

14. Wara DW, Ammann AJ: Thymic cells and humoral factors as therapeutic agents. Pediatrics 1976; 57:643-646

How About Organizing 'Friends of Medicine'?

THE MEDICAL PROFESSION and organized medicine seem to find themselves in a paradoxical position with respect to public opinion and public support. Physicians and even organized medicine continue to rate very well in public opinion polls that purport to measure such things as trust, integrity and performance. Yet in their public image, as this is reflected in the informational media and in public rhetoric, they seem to be depicted too often as self-serving, noncaring, unduly rich and dedicated to personal and professional self-aggrandizement. From this it would seem that it is public image rather than public opinion that has brought about a progressive deterioration in the way the medical profession and organized medicine are viewed in the political arena. Somehow the favorable public opinion of trust, integrity and good performance has lost much of its political clout and the public image (which like all images is unreal) seems to be having a growing impact upon the economic and political fortunes of the profession. This is a matter of some concern since so many issues affecting health and patient care are now being decided in the political arena.

In our political system the votes are what decide the issues. Physicians are not and never will be a significant voting block. Political action committees (the PAC's) and the devoted support of medical society auxiliaries have greatly strengthened the profession's hand. But these do not bring the strength of those responsible for the favorable public opinion polls fully to bear either to influence the profession's public image or the fortunes of physicians and their patients in the crucibles of political decision. Some ways need to be found to strengthen the voter base of the medical profession and patient care. How is this to be done? There are many patients, former patients, and friends and families of patients who could rally around physicians and their medical societies to become more organized "Friends of Medicine" for community and political action in behalf of the medical profession and better patient care. Organized groups of such "friends" are nothing new, especially in the health care field, and they make possible an enormously expanded base of community and